Case Presentation

By

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welcome

Patient Story

1ST Part

2nd Part

Patient Story

1ST Part

History

65 years
Female

Gradual ,progressive Dyspnea &Pallor

Sr Cr=5.5 mg/dl
Urea=101 mg/dl
Hb=6.3 g/dl

Menopause 15 years ago.
No special habits of medical importance.
No past history of medical diseases
Irrelevant family history

Examination

- The patient is conscious, average body built (weight: 65Kg- Height: 148cm BMI: 28.8).
- pulse= 110 b/m regular
- RR= 22 c/m
- Temp= 37 C
- Bp : 170/100 mmHg
- H&N: Marked pallor, no jaundice, or congested neck veins.
- Chest & Heart: Mild decrease air entry bilateral.
- Abdomen: No organomegaly or ascites.
- Extremities: Bil mild LL oedema.
- No lymphadenopathy.

Labs

Labs	Results
Sr Cr	6 mg/dl
Blood urea	115 mg/dl
Hb	6.2 g/dl normochromic, normocytic
plateletes	259,000/cmm
WBCs	9200/cmm
PH	7.2
HCO3	10 mEq/l
Pco2	15 mmHg
Na	140 mEq/l
K	5.3 mEq/l

Labs

Labs	Results
Urine analysis:	Pus cells: 5-6/HPF RBCs:**10-15**/HPF Protein: **+3** No casts crystals not seen
24 hour urinary protein collection	**1.3 g/24h**
Cholesterol: **Triglycerides**	**180 mg/dl** **170 mg/ dl**
Uric acid	**7.1 mg/dl**
Serum albumin	**3.7 g/L**

Labs

Labs	Results
Ca	**8.2 mg/ dl**
Po4	4.9 mg/ dl
PTH	95 pg /ml
ANA	-ve
Anti Ds DNA	-ve
C3	**Less than 10 mg/dl** (10-40)
C4	**67 mg/dl** (90-180)
Hepatitis C antibody	-ve
Hepatitis B s antigen	-ve
HIV antibodies	-ve
ANCA	-ve

Imaging

Abdominal US

Mild bright hepatomegally.
Bilateral mild pleural effusion.
Bilateral Grade I non obstructive nephropathy

- *Renal biopsy was done*

Initial management

The patient received conservative treatment :

- CCB, Blood transfusion, Correction of metabolic acidosis, Calcium carbonate.

Sr Cr=6.5 mg/dl → SrCr=7.2mg/dl → Sr Cr=8.5mg/dl

HD

End of 1st part

- Waiting for biopsy results, the patient wanted to be discharged for follow up at TNU outpatient clinic. However, she disappeared for about 8 months where she continued dialysis at another center.

Patient Story

2nd part

- After 8 months, the patient came back for the possibility of reducing dialysis frequency as her monthly renal functions persistantly decreased.

(Sr Cr 2.5 mg/dl, Urea 64 mg/dl)

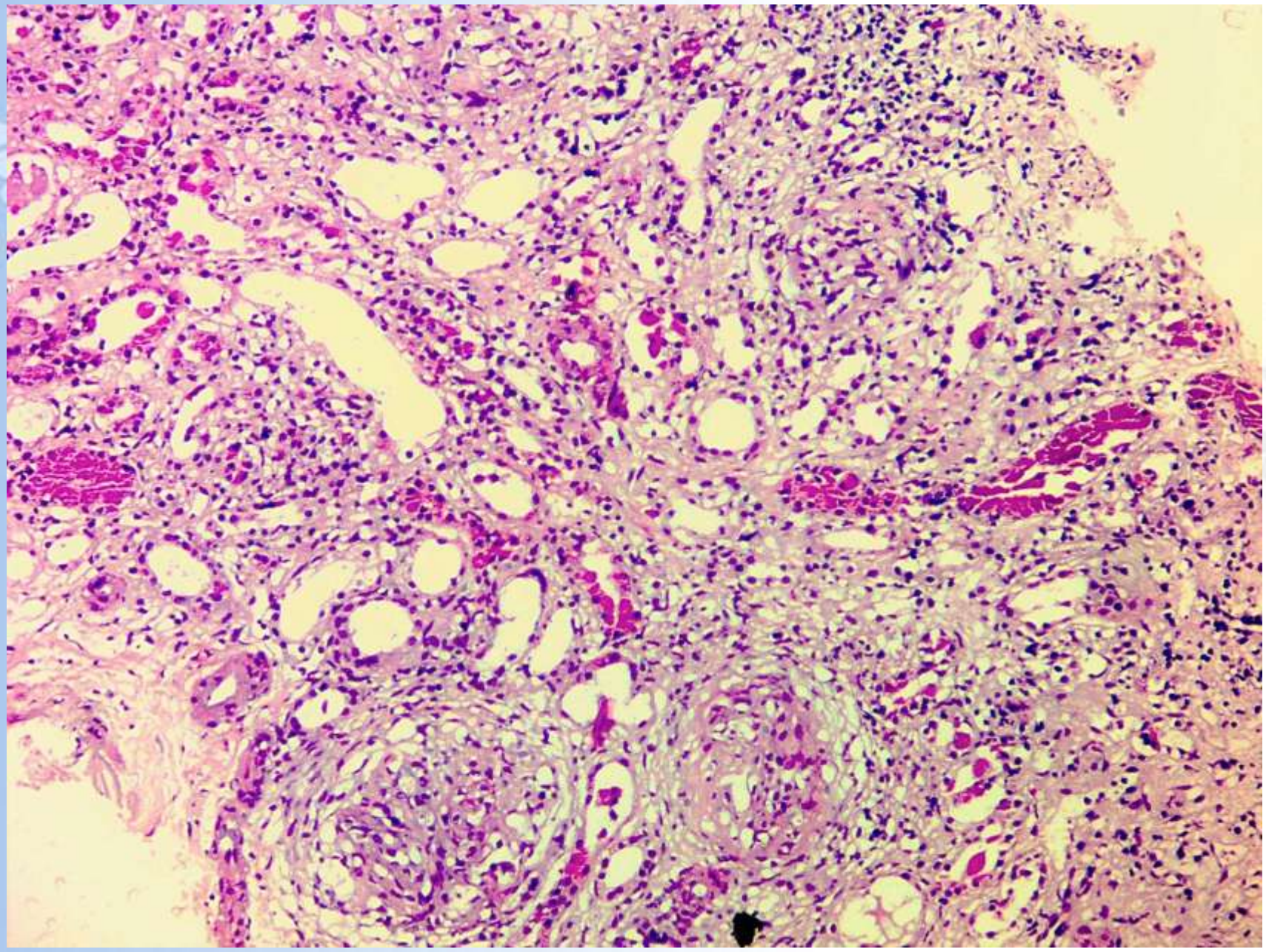
Examination

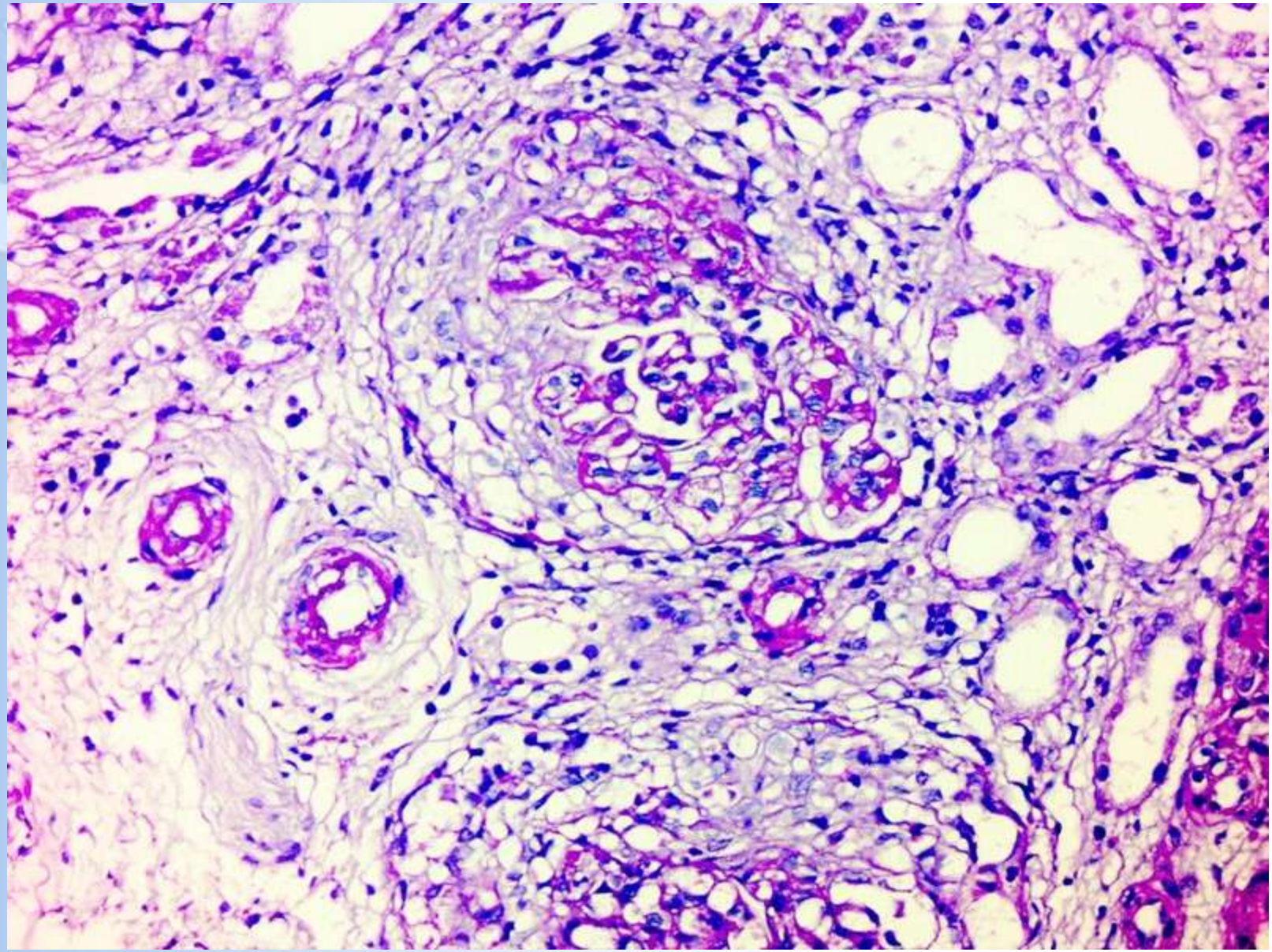
- **Dyspnea,** average body built (weight: 60Kg-Height: 148cm BMI: 26.6)
- Bp : 130/80 mmHg.
- H&N: **marked pallor**, no jaundice, or congested neck veins.
- Chest & Heart: Free.
- Abdomen: No organomegaly or ascites.
- Extremities: No LL oedema.
- No lymphadenopathy.

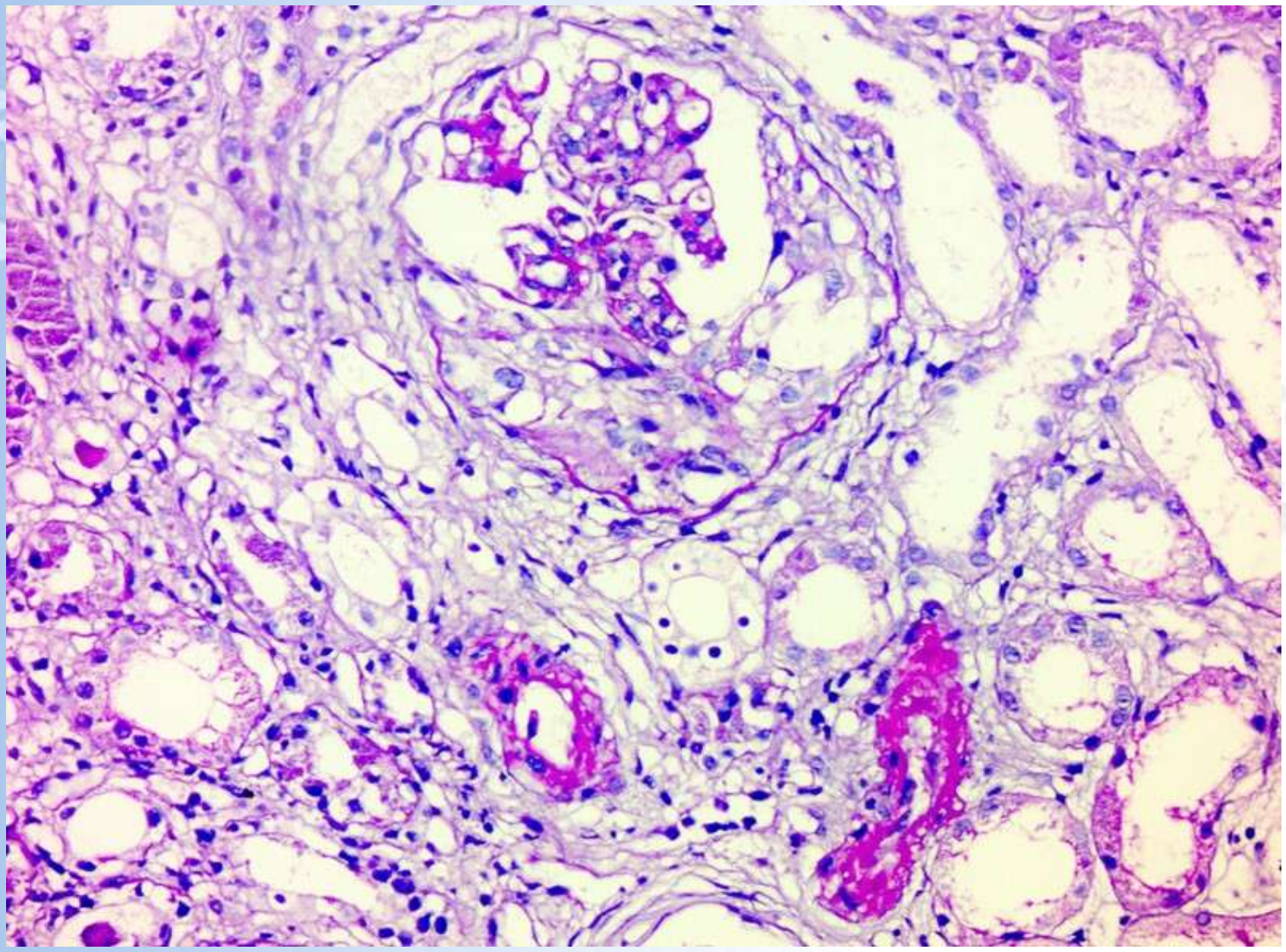
New Labs

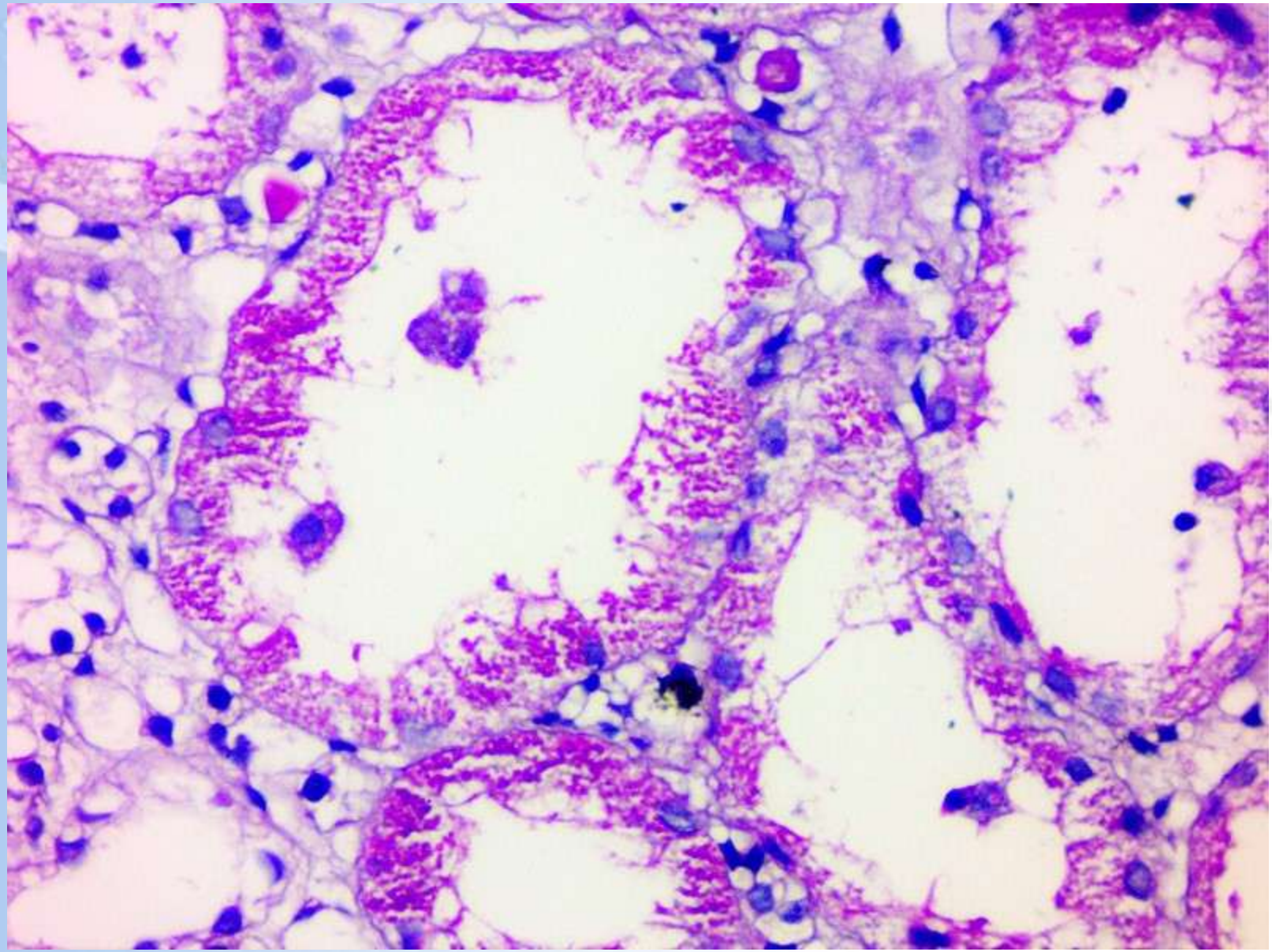
Labs	Results
Sr Cr	2.5 mg/dl
Blood urea	64 mg/dl
Hb	5.9 g/dl normochromic, normocytic
plateletes	151,000/cmm
WBCs	4000/cmm
Ca	8.5 mg/dl
Po4	4.7 mg/dl
PTH	167 pg/ml
Ferritin	1000 ng /ml

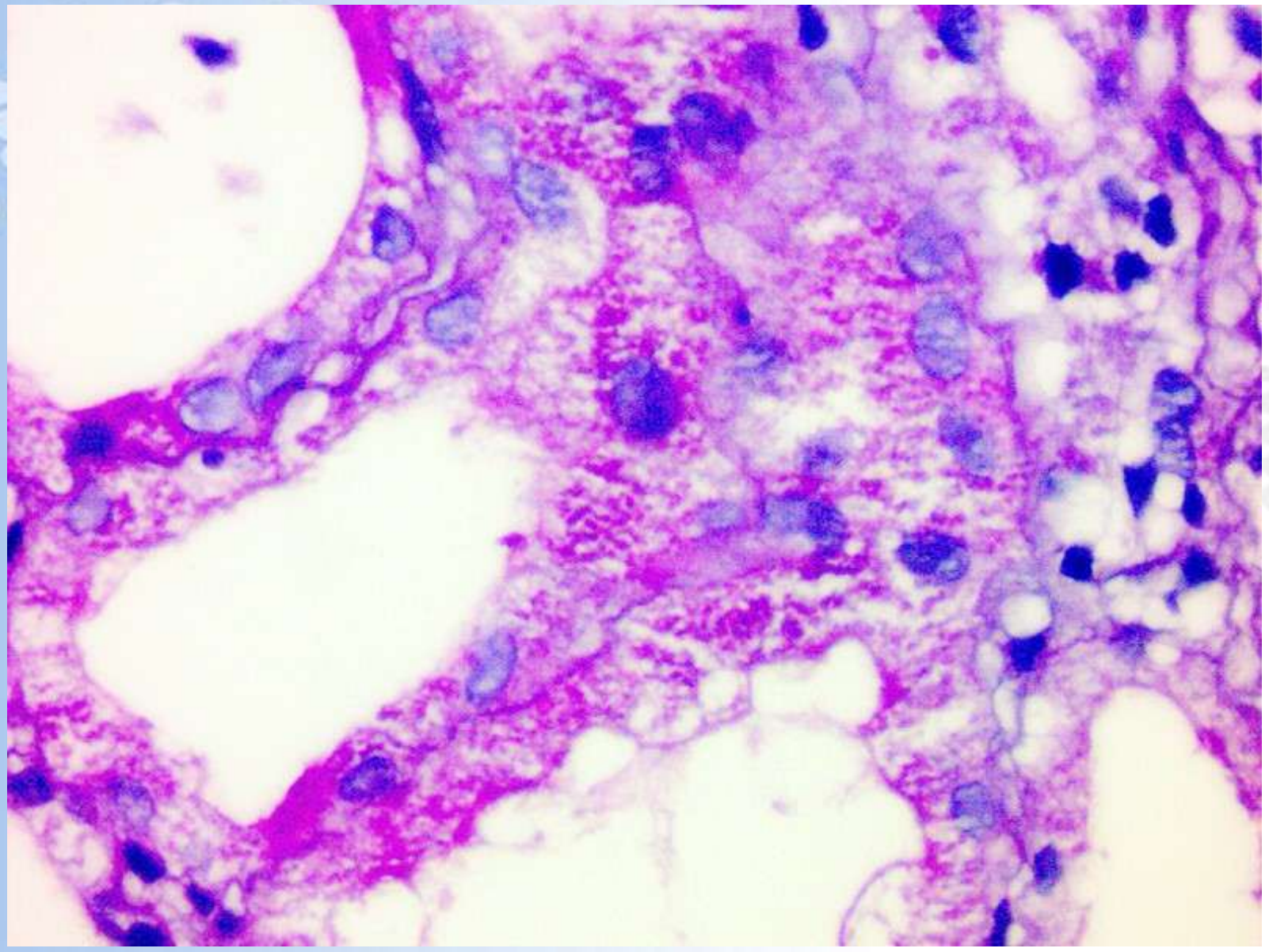
- **Ranal histopathology**

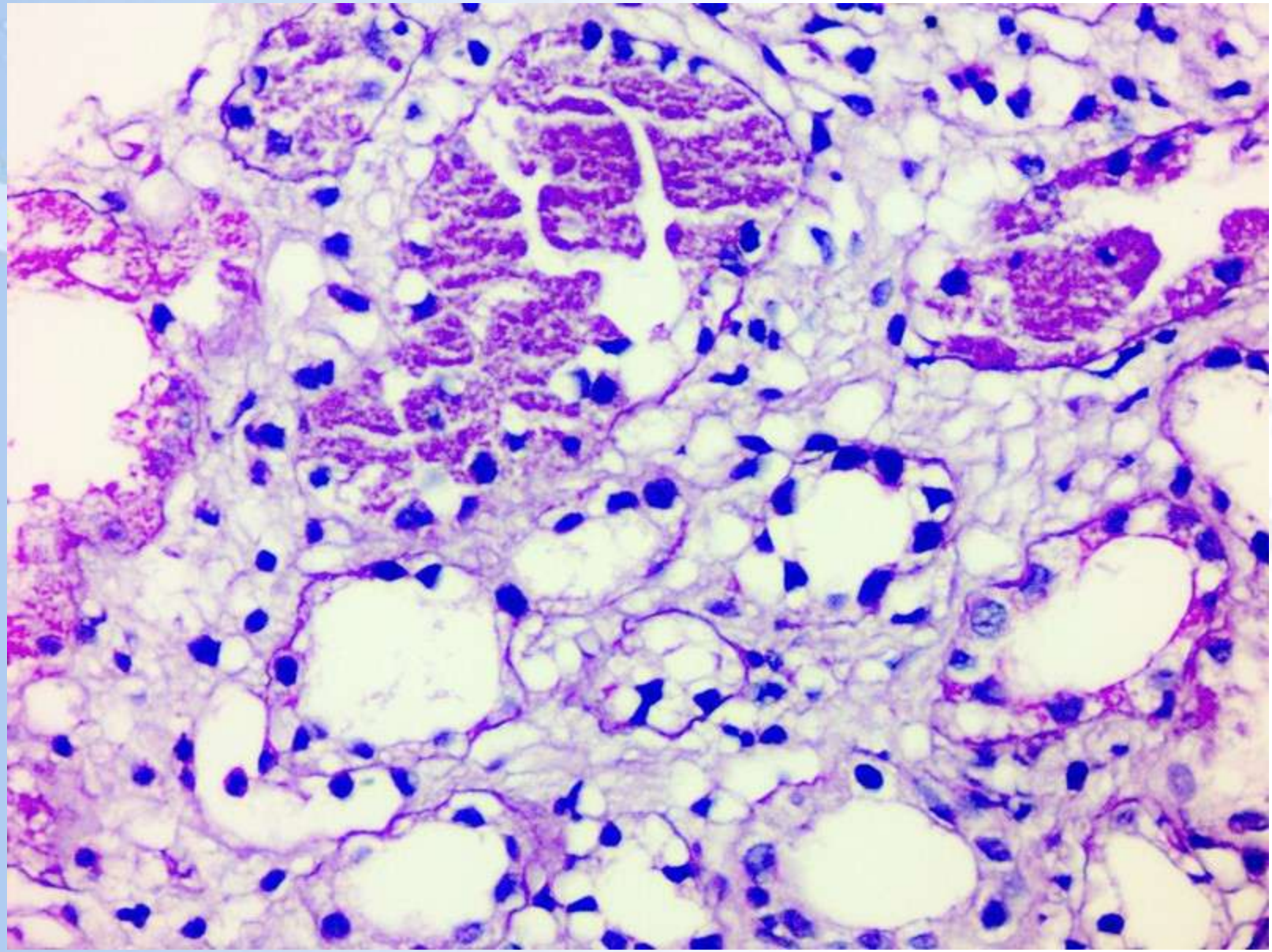


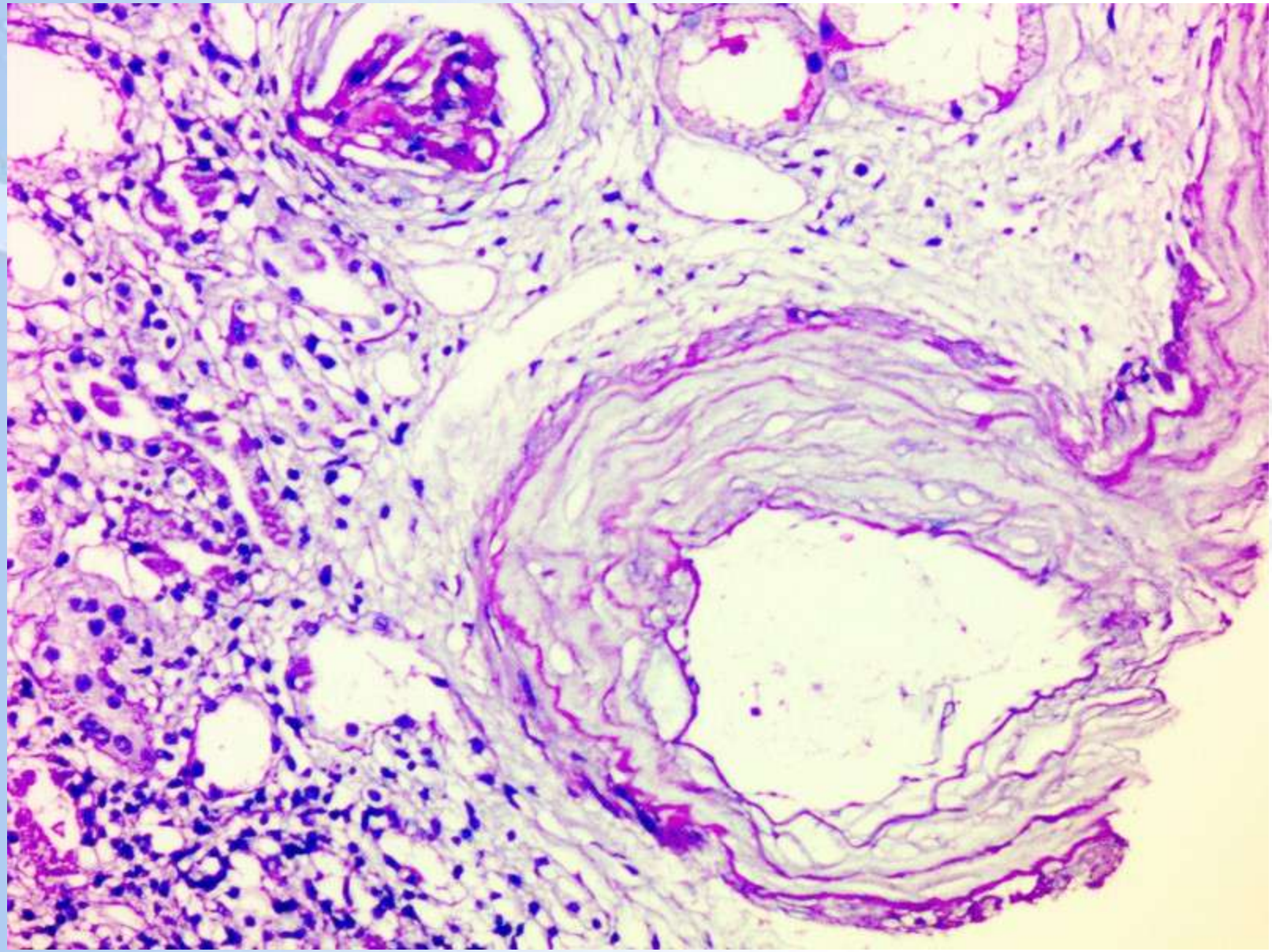












Medications

- CCB
- Calcium carbonate.
- Alphacalcidol
- Dialysis frequency was reduced.
- Epoietin alpha dose gradually increased up to 4000 U 4 times /w.

After 6 Weeks

Labs	Results
Hb	6.2 g/dl normochromic, normocytic
plateletes	150,000/cmm
WBCs	4200/cmm
ESR	1ST hour 35 mm
LDH	245
RF	**+ve**

What is the cause of resistance?

Causes of ESA Hyporesponsiveness

- Iron deficiency ** *most common* **
- Infection
- ACE inhibitors
- Hyperparathyroidism – bone marrow fibrosis
- Inadequate dialysis.
- B12 & Folate deficiency
- Malignancies, including multiple myeloma
- Aluminium toxicity

1- iron defeciency

- Serum ferritin: › 1000
- Serum iron: 0.67 (0.4-1.3 ug/ml)
- Transferrin saturation: 50%

No iron defeciency

2- Infection

- Clinically free.
- CRP: Negative.

No Infection

3-ACE inhibitors

- Patient was maintained on calcium channel blocker treatment.

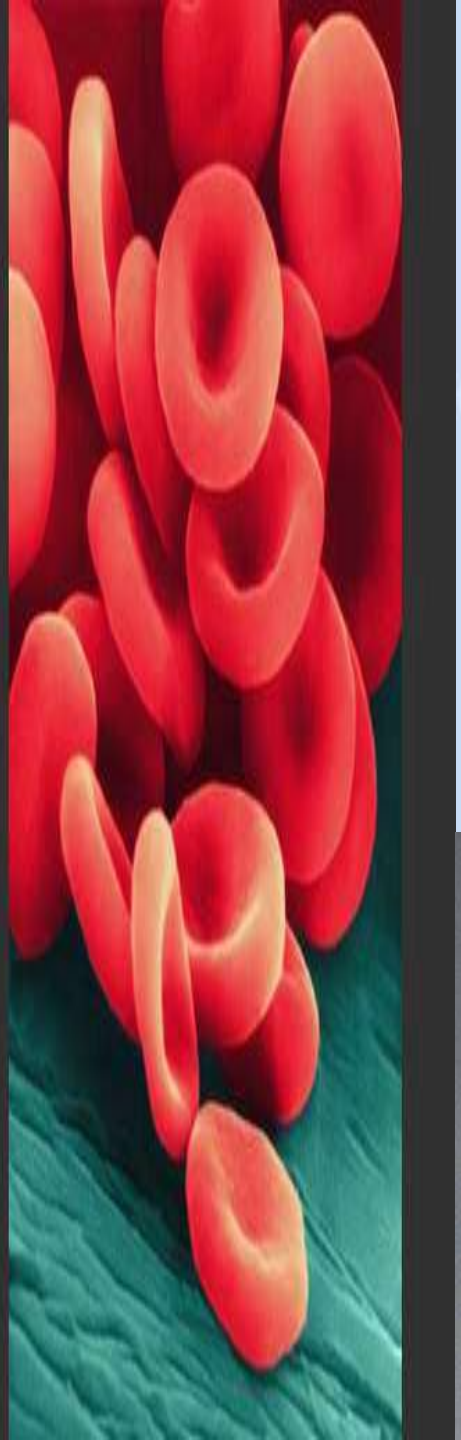
No ACE inhibitors

4-Hyperparathyroidism
BM fibrosis

- PTH level: 167 pg /ml.
- Serum calcium: 8.6 mg/dl.
- Serum phosphorus: 4.6 mg/dl.

5-Vitamin B12 folic acid deficiency

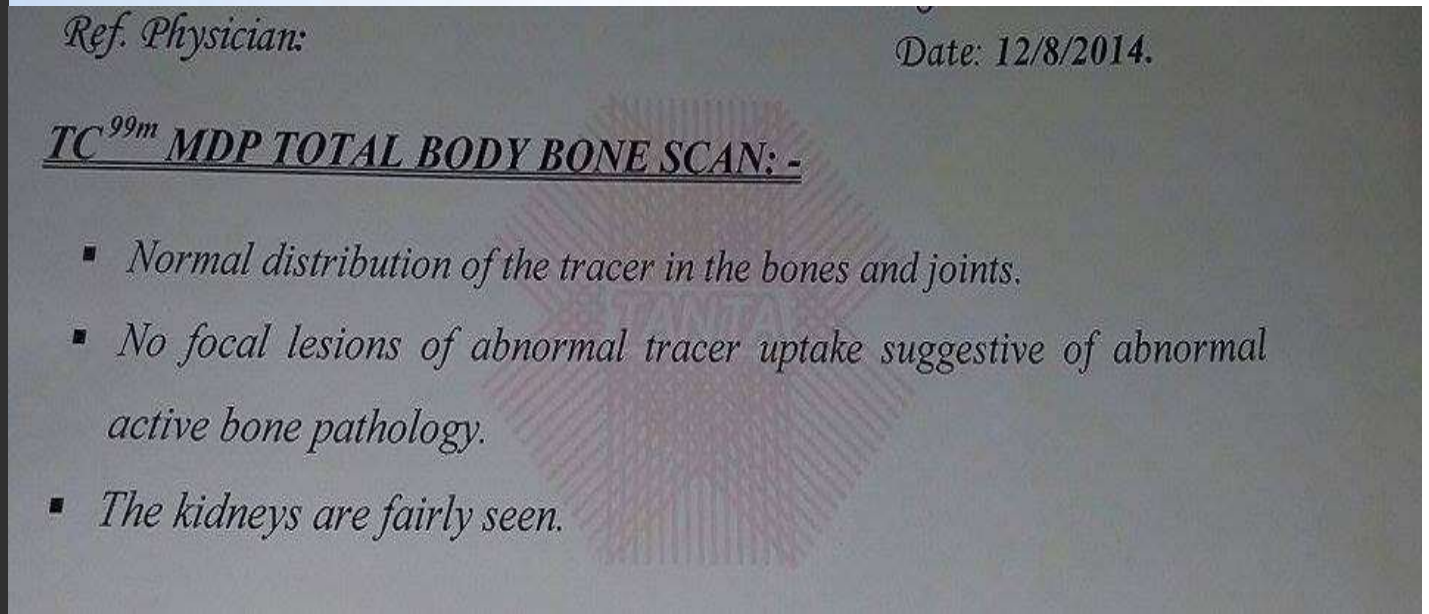
- Normochromic normocytic.
- Reticulocytic count= 3%.
- Patients already received vitamin B 12 injection.



Occult malignancy

Multiple myeloma

- Plasma protein elecrophoresis:-ve for M band
- Negative Bence Jones protein in urine.

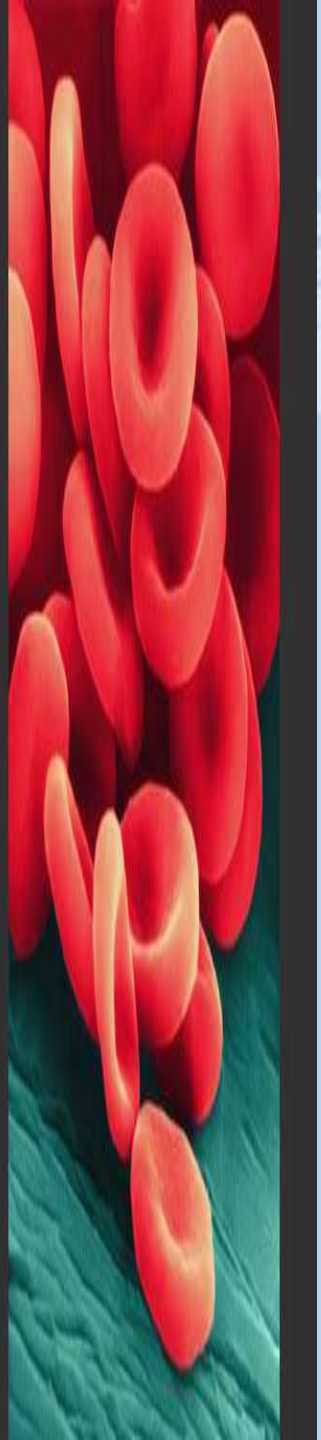


Ref. Physician:

Date: 12/8/2014.

TC^{99m} MDP TOTAL BODY BONE SCAN: -

- *Normal distribution of the tracer in the bones and joints.*
- *No focal lesions of abnormal tracer uptake suggestive of abnormal active bone pathology.*
- *The kidneys are fairly seen.*



Bone marrow aspiration

- Hypocellular bone marrow with normoblastic reaction (as a response to anemia), relative depression of granulopoiesis and depressed thrombopoiesis
- No malignant or leukemic infiltration
- This hypocellular BM favour the diagnosis of drug induced bone marrow hypoplasia for follow up????

- Normal cardiac size.
- Clear both costo-phrenic angles.
- No detectable hilar masses or lymphadenopathy.
- No mediastinal mass or enlarged lymph nodes
- Clear both cardio-phrenic angles.

Examination: CT Abdomen and Pelvis USING MULTI-DETECTOR CT (AQUILION 16 SLICE) WITH ORAL CONTRAST.

- **Both kidneys are relatively small in size with no stones or back pressure changes.**
- **Mild enlarged liver with no masses or focal lesions.**
- No intra-hepatic biliary radical dilatation seen.
- No ascites.
- Average size spleen with no masses or focal lesion.
- Average size gall bladder, no masses, and no stones.
- Free para-aortic, pre-caval regions with no lymph node enlargement.
- Average caliber bowel loops with no detectable masses.
- Normal size and wall thickness of the UB with preserved perivesical fat.
- Cuts taken in the lower chest are free.

MUCH OBLIGED
Dr/ Mohammed Elshafey(Prof).

£

What is the next step?

- **Bone marrow biopsy was done.**

What do you expect in BM biopsy ?

Name MRS. AMIENA ABDEL KADER 272685

BONE MARROW CORE BIOPSY EXAMINATION

Specimen: 1.2 cm core biopsy from iliac bone.

Comment: The bone marrow is hypercellular for age (average cellularity ~ 70%) due to infiltration by about 50% abnormal lymphoid cells. They are medium sized with clumped nuclear chromatin. They are scattered interstitially in addition to two large lymphoid nodules. The marrow hematopoietic elements are some how preserved especially megakaryopoiesis which is increased with small dysplastic forms. In addition the marrow is affected with evident fibrous tissue deposition distorting the normal architecture and cellular morphology. No evidence of granulomas or non-haematopoietic infiltrations.

Immunohistochemistry:

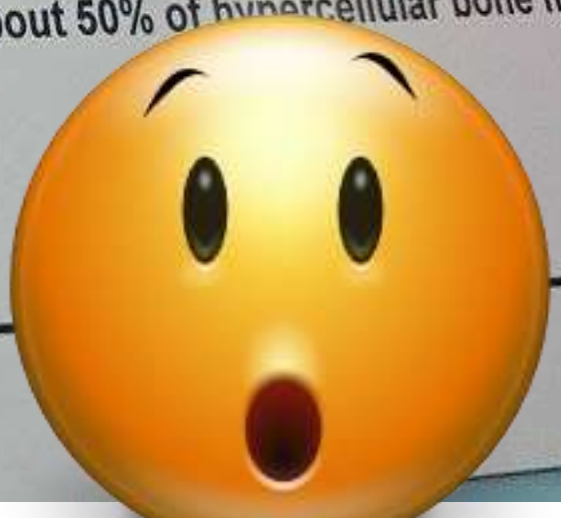
CD20: Strong positive on the lymphocytes in the lymphoid aggregates. Inaddition to, scattered positive cells interstitially.

CD3: Scattered CD3 positive T-cells. Negative on the lymphocytes in the lymphoid aggregates.

CD138: Scattered CD138+ plasma cells (about 5% of the cells).

Conclusion: Picture of non-Hodgkin lymphoma infiltrating about 50% of hypercellular bone marrow. fibrosis is present.

Five stained slides were given to the patient.



6 cycles of CHOP

BONE MARROW EXAMINATION

Gross:

- Core biopsy in solution.

Data :

- Follow up after chemo - NHL.

Morphology:

- Marrow is hypocellular , show residual neoplastic small mature lymphocytes in follicles and interstitial , mild interfollicular fibrosis is present .

Diagnosis:

- Residual low grade NHL , about 20 % of present cellularity

Slide & block enclosed

Reported & signed by:
Prof Refaat Gab Allah
Hematologist

Is there a relation between GN and NHL in this patient ?

Take Home Messages

Malignancy -GN

- The association of GN and malignancy is regarded as one of the examples of broad-phenomenon disorders.
- The more commonly associated neoplasia are carcinoma of the lung or the GIT and Hodgkin's disease (HD).
- The pathology is usually membranous nephropathy in patients with solid tumors and amyloidosis or MC nephropathy in HD.

- RAULT R, et al., Glomerulonephritis and non-Hodgkin's lymphoma: a report of two cases and review of the literature. Am J Kidney Dis 1992;20:84±89.

Lymphoma -GN

- Renal involvement in non-Hodgkin lymphoma (NHL) has been reported previously, including GN and acute kidney injury (AKI), particularly with B cell type NHL.

- Glomerular involvement may preceded, coexisted with or even followed the diagnosis of lymphoma by several years.

- Da'as N:Kidney involvement and renal manifestations in non-Hodgkin's lymphoma and lymphocytic leukemia: a retrospective study in 700 patients. Eur J Haematol ,2001 , 158:164-67.

Lymphoma -GN

- Glomerular lesions in patients with NHL vary widely and depend on the stage of lymphoma.

- Proliferative lesions are more common in NHL compared with HL, and may account for up to 30% of glomerular diseases.

- Da'as N:Kidney involvement and renal manifestations in non-Hodgkin's lymphoma and lymphocytic leukemia: a retrospective study in 700 patients. Eur J Haematol ,2001 , 158:164-67.

Malignancy	Glomerular Lesions	Important Points
ALL	MCD FSGS	• Proteinuria can be due to lysozymuria induced tubular damage • More often glomerular damage precedes malignancy • Predominantly seen in children
AML	MCD FSGS MPGN Mesangioproliferative GN	• Proteinuria can be due to lysozymuria-induced tubular damage • Possible association with oncomavirus antigens
CLL	MCD FSGS Membranous nephropathy MPGN IgG kappa and lambda Amyloidosis (AA) Crescentic GN Immunotactoid GN Mesangioproliferative GN	• Associated with autoimmune disease • Infiltration in 90% of patients (asymptomatic and symptomatic)
CML	MCD Membranous nephropathy MPGN	• Very rare with primary disease • Associated with interferon- α therapy and posthematopoietic stem cell transplantation
MDS/MPN	**MDS**: Membranous nephropathy Mesangioproliferative GN Amyloidosis (AL) **PV**: FSGS Mesangioproliferative GN IgA nephropathy **ET**: FSGS Mesangioproliferative GN **MF**: FSGS Mesangioproliferative GN Amyloidosis **CMML**: Amyloidosis (AL)	• MPN glomerulopathy has been described in patients with PV, ET, and MF. Includes a collection of histological findings: mesangial sclerosis and hypercellularity, segmental sclerosis, chronic thrombotic microangiopathy, and intracapillary hematopoietic cell infiltration
HL	MCD FSGS Amyloidosis (AA) Crescentic GN	• Occur late in disease • No correlation with disease progression or severity • Associated with elevated VEGF-25,TGF-βexpression in models
NHL	MCD FSGS Membranous nephropathy MPGN Mesangioproliferative GN Crescentic GN Amyloidosis (AL) IgA nephropathy Immunotactoid GN Fibrillary GN	• Occur early in disease • Severity mirrors disease progression • Associated with hepatitis C and Epstein-Barr viral infections

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Kidney involvement and renal manifestations in non-Hodgkin's lymphoma and lymphocytic leukemia: a retrospective study in 700 patients

Table 1. Renal failure in patients with NHL in this study

Cause	No. of patients
Direct effects (lymphoma)	19
Infiltration of kidney	5
Obstruction	14
Indirect effects (paraneoplastic)	7
Glomerulonephritis	4
Paraproteinemia	1
Cryoglobulinemia	2
Therapy-related	15
Tumor lysis syndrome	4
Cytoxan-induced cystitis	4
Infection/nephrotoxic drugs	7
Unrelated to NHL	13
Unknown	12

Renal Involvement in Non-Hodgkin Lymphoma: Proven by Renal Biopsy

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National Clinical Research Center of Kidney Diseases, Jinling Hospital, Nanjing University of Medcine, Nanjing, China

Abstract

Aims: To determine the spectrum of renal lesions in patients with kidney involvement in non-Hodgkin's lymphoma (NHL) by renal biopsy.

Methods: The clinical features and histological findings at the time of the renal biopsy were assessed for each patient.

Results: We identified 20 patients with NHL and renal involvement, and the diagnosis of NHL was established following the kidney biopsy in 18 (90%) patients. The types of NHL include the following: chronic lymphocytic leukemia/small lymphocytic lymphoma (n = 8), diffuse large B-cell lymphoma (n = 4), T/NK cell lymphoma (n = 3), lymphoplasmacytic lymphoma (n = 2), cutaneous T-cell lymphoma (n = 1), mucosa-associated lymphoid tissue lymphoma (n = 1) and mantle cell lymphoma (n = 1). All presented with proteinuria, and 15 patients had impaired renal function. The pathological findings included (1) membranoproliferative glomerulonephritis-like pattern in seven patients; (2) crescent glomerulonephritis in four; (3) minimal-change disease in three, and glomeruli without specific pathological abnormalities in three; (4) intraglomerular large B-cell lymphoma in one; (5) intracapillary monoclonal IgM deposits in one; (6) primary diffuse large B-cell lymphoma of the kidneys in one; and (7) lymphoma infiltration of the kidney in eight patients.

Conclusion: A wide spectrum of renal lesions can be observed in patients with NHL, and NHL may be first proven by renal biopsies for evaluation of kidney injury or proteinuria. Renal biopsy is necessary to establish the underlying cause of renal involvement in NHL.

Table 3. Renal biopsy findings

	Glomerular Disease	Infiltrating cells		Immunofluorescence						
		Glomerular	PTC	IgG	IgA	IgM	C3	C1q	κ	λ
1	Crescent GN	>5	Y	-	-	-	-	-	-	-
2	Crescent GN	2–3	Y	-	-	-	-	-	-	-
3	NSPA	2–3	No	+	-	+	-	-	-	-
4	MCD	2–3	Y	-	-	-	-	-	-	-
5	NSPA	>3	Y	++	-	-	++	++	-	+
6	MPGN	>10	Y	-	-	+	+	+	-	-
7	Crescent GN	>5	Y	++	-	-	-	-	-	+
8	Crescent GN	>5	Y	++	+	+	++	++	+	+
9	MPGN	>10	Y	++	+	++	++	+	++	+
10	MCD	3–5	Y	-	-	-	-	-	-	-
11	MCD	3–5	Y	-	-	-	-	-	-	-
12	ICMDD	3–5	Y	-	-	++	-	-	++	-
13	No glomerular	ND	Y	-	-	-	-	-	-	-
14	Lymphoma	ND	Y	-	+	+	-	-	-	-
15	MPGN	>10	Y	++	+	++	+	++	+	++
16	MPGN	>10	No	++	++	-	++	-	+	+
17	NSPA	3–5	Y	-	-	-	-	-	-	-
18	MPGN	>5	Y	-	++	-	++	-	+	-
19	MPGN	>10	No	++	-	-	++	++	-	+
20	MPGN	>10	No	++	++	-	++	-	++	+

Lymphoma -GN

The pathogenesis of NHL-associated GN is poorly understood. However, the mechanisms of paraneoplastic GN includes:

- Dysfunctional cytokine production leading to **immune complex deposition** and cellular proliferation.
- **Autoimmune mechanisms** and T- lymphocyte dysfunction.
- **Cryoglobulinaemia**: either immune-complexes (type II) or remain of undetermined nature (type I).
- **The secreted M-component** can injure glomeruli through a noncryoglobulin- mediated mechanism.

Lymphoma -GN

Other causes of renal impairment in the setting of lymphoma is usually due to:

- Direct infiltration of the kidney by malignant cells.
- Obstruction of ureters by tumor mass.
- Renal artery or vein thrombosis.
- Sepsis, hemolysis, paraproteinemia or amyloidosis
- Therapy-related causes of renal failure include radiation nephritis , tumor lysis syndrome, chemo-therapeutic agents or antibiotics.

THNAKS

- **Tanta Hematology Unit**

Thank you